

Health Technology Briefing March 2023

Durvalumab with carboplatin and paclitaxel with or without olaparib for newly diagnosed advanced or recurrent endometrial cancer

Company/Developer

AstraZeneca UK Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 29610

NICE TSID: 11856

UKPS ID: 668738

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Durvalumab in combination with carboplatin and paclitaxel and/or olaparib is currently in clinical development for the treatment of endometrial cancer. Endometrial cancer, also referred to as uterine or womb cancer, is the presence of cancer cells on the lining of the womb. It is the 4th most common cancer among women in the UK. Symptoms of endometrial cancer include abnormal bleeding from the vagina, pain during sex, and lower back pain. Increasing age and higher levels of oestrogens are some of the risk factors associated with endometrial cancer. There is an unmet need for advanced treatments that offer survival benefits among endometrial cancer patients.

Durvalumab is a type of protein (monoclonal antibody) administered by intravenous infusion to increase the ability of the immune system to kill cancer cells. Medicinal products with similar mechanism of action have shown enhanced antitumour activity. If licensed, durvalumab in combination with carboplatin and paclitaxel and/or olaparib will offer an additional treatment option for endometrial cancer patients.

Proposed Indication

Maintenance therapy for newly diagnosed advanced or recurrent endometrial cancer.¹

Technology

Description

Durvalumab (Imfinzi, MEDI4736) is a fully human, immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that selectively blocks the interaction of programmed cell death ligand-1 (PD-L1) with PD-1 and CD80. Expression of PD-L1 protein is an adaptive immune response that helps tumours evade detection by the immune system. The selective blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances antitumour immune responses and increases T-cell activation.²

In the phase III clinical trial (DUO-E, NCT04269200), patients were randomised to carboplatin and paclitaxel IV (intravenous) with durvalumab IV 1120 milligrams (mg) once every 3 weeks for 6 cycles followed by durvalumab IV 1500mg once every 4 weeks and placebo tablets twice daily; or carboplatin and paclitaxel with durvalumab IV 1120mg once every 3 weeks for 6 cycles followed by durvalumab IV 1500mg once every 4 weeks and olaparib 300mg tablets twice daily.³

Key Innovation

PD-L1 protein acts to switch off immune cells that would otherwise attack the cancer cells.⁴ Durvalumab attaches to and blocks the effects of PD-L1, thereby enhancing the immune system's ability to attack the cancer cells and slow down disease progression.⁴ Previous clinical trials have demonstrated antitumour activity of PD-L1 blockers such as durvalumab.³

There is an unmet need for advanced treatments that offer progression-free survival (PFS) and overall survival benefits among endometrial cancer patients.³ If licensed, durvalumab in combination with carboplatin and paclitaxel and/or olaparib will provide an additional treatment option for patients with endometrial cancer.

Regulatory & Development Status

Durvalumab as a monotherapy has Marketing Authorisation in the UK for the treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC) in adults whose tumours express PD-L1 on ≥1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy. It is also licensed in combination with etoposide and either carboplatin or cisplatin for the first line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC). Durvalumab in combination with gemcitabine and cisplatin is indicated for the first line treatment of adults with locally advanced, unresectable, or metastatic biliary tract cancer (BTC).²

Durvalumab is in phase II and III clinical development for several other indications such as:⁵

- Lung Cancer
- Breast Cancer
- Renal Cell Cancer
- Bladder Cancer
- Oesophageal Cancer

Patient Group

Disease Area and Clinical Need

Endometrial cancer, also known as uterine or womb cancer, is the presence of cancer cells on the lining of the womb (endometrium).⁶ Advanced uterine cancer refers to cancer that has spread into the surrounding tissues or organs and is unlikely to be treatable.⁷ Recurrent uterine cancer refers to cancer that has returned after primary treatment.⁸ The most common symptom of endometrial cancer is abnormal bleeding from the vagina.⁶ Other symptoms of endometrial cancer include pain during sex, swelling between the stomach and hip bone, and lower back pain.⁹ Although the specific cause of endometrial cancer is unknown, development of the disease has been associated with higher levels of oestrogen.¹⁰ Age is also a significant risk factor, with most cases occurring in women aged between 40 and 70 years old.¹⁰ Other risk factors include being overweight or obese, previous history of taking tamoxifen (breast cancer medication), women who have not had children, polycystic ovary syndrome and high insulin levels.¹⁰

Endometrial cancer is the 4th most common cancer among women in the UK.¹⁰ There were approximately 9,700 new cases in the UK between 2016 and 2018.¹¹ The age-standardised incidence rate in the UK for endometrial cancer (2016-2018) was 29.7 per 100,000 in females.¹¹ In England, between 2013-2017, the age-standardised average 5-year overall survival rate among women was 76%.¹² From 2017-2019 in England, the mortality rate of endometrial cancer was 2,005 per 100,000 female population.¹³ In England, 2021-22, there were 18,420 finished consultant episodes (FCE) and 17,317 admissions for endometrial cancer (ICD-10 code C54.1) which resulted in 27,566 FCE bed days and 9,644 day cases.¹⁴

Recommended Treatment Options

NICE currently recommends the following therapies for the treatment of endometrial cancer:

- Laparoscopic hysterectomy.¹⁵
- Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency.¹⁶

The European Society for Medical Oncology (ESMO) also recommends carboplatin in combination with paclitaxel for the treatment of endometrial cancer.¹⁷

Clinical Trial Information

<p>Trial</p>	<p>NCT04269200, EudraCT 2019-004112-60; A Randomised, Multicentre, Double-blind, Placebo-controlled, Phase III Study of First-line Carboplatin and Paclitaxel in Combination With Durvalumab, Followed by Maintenance Durvalumab With or Without Olaparib in Patients With Newly Diagnosed Advanced or Recurrent Endometrial Cancer (DUO-E) Phase III- Recruiting Location(s): Eight EU countries, USA, Canada and other countries Primary completion date: September 2023</p>
<p>Trial Design</p>	<p>Randomised, parallel assignment, double-blind, placebo-controlled</p>
<p>Population</p>	<p>N=699 (estimated); female adults (≥18 years old); histologically confirmed diagnosis of endometrial cancer (must be newly diagnosed stage III, IV, or recurrent)</p>

Intervention(s)	Durvalumab IV with carboplatin and paclitaxel IV once every 3 weeks for 6 cycles followed by durvalumab IV once every 4 weeks + olaparib orally twice daily. ³
Comparator(s)	Carboplatin and paclitaxel and placebo
Outcome(s)	<p>Primary Outcome measures:</p> <ul style="list-style-type: none"> Progression-free survival for Arm B vs Arm A and Arm C vs Arm A [Time Frame: Up to 4 years] <p>See trial record for full list of other outcomes</p>
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The NHS indicative price (hospital only) of durvalumab concentrate for solution for infusion vials is £592 for 120mg/2.4ml and £2,466 for 500mg/10ml.¹⁸

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Dostarlimab with carboplatin and paclitaxel for treating recurrent advanced endometrial cancer [ID3968]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Pembrolizumab with lenvatinib for previously treated advanced or recurrent endometrial cancer [ID3811]. Expected date of March 2023.
- NICE technology appraisal. Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (TA779). March 2022
- NICE interventional procedures guidance. Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer [IPG356]. September 2010

NHS England (Policy/Commissioning) Guidance

- NHS England 2013-2014. Standard Contract for Complex Gynaecology: Specialist Gynaecological cancers. E10/S/f
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.

Other Guidance

- European Society for Medical Oncology. Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. 2022.¹⁷
- British Gynaecological Cancer Society (BGCS). Uterine Cancer Guidelines: Recommendations for Practice. 2021.¹⁹
- European Society of Gynaecological Oncology (ESGO), the European Society for Radiotherapy and Oncology (ESTRO), and the European Society of Pathology (ESP). ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. 2020.²⁰

Additional Information

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